From the Departments of Pharmacology and Integrative Biology and Physiology, The University of Minnesota

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High Fat Diet Induced Obesity as a Model for Cardiac and Metabolic Dysfunction

Sabrine R. Garrison, BA, Naixin Zhang, MS, Chastity L. Healy, BS, and Timothy D. O'Connell, PhD

ABSTRACT

The purpose of this study is to investigate if high fat diet (HFD) induced obesity alone can act as a model for both cardiac and metabolic dysfunction in a mouse model. We measured body weight, energy consumption, body composition, and fasting glucose levels in mice fed high fat diet and a regular control diet (NCD). The HFD was composed of 30% sucrose and 41% fat, and was intended to mimic what is considered a standard western human diet which is high in fat and sugar. We hypothesize that mice fed high fat diet will have an obese phenotype characterized by increased body weight, fat mass and fasting glucose levels. In addition, the obese phenotype will be accompanied by early signs of cardiac dysfunction. Preliminary data from this study indicates that high fat diet does induce an obese phenotype, characterized by increase body weight, fat mass/percentage, and increased fasting glucose levels. Ultimately, this is an active study and further investigation will be done to identify if high fat diet alone is sufficient to induce cardiac dysfunction.

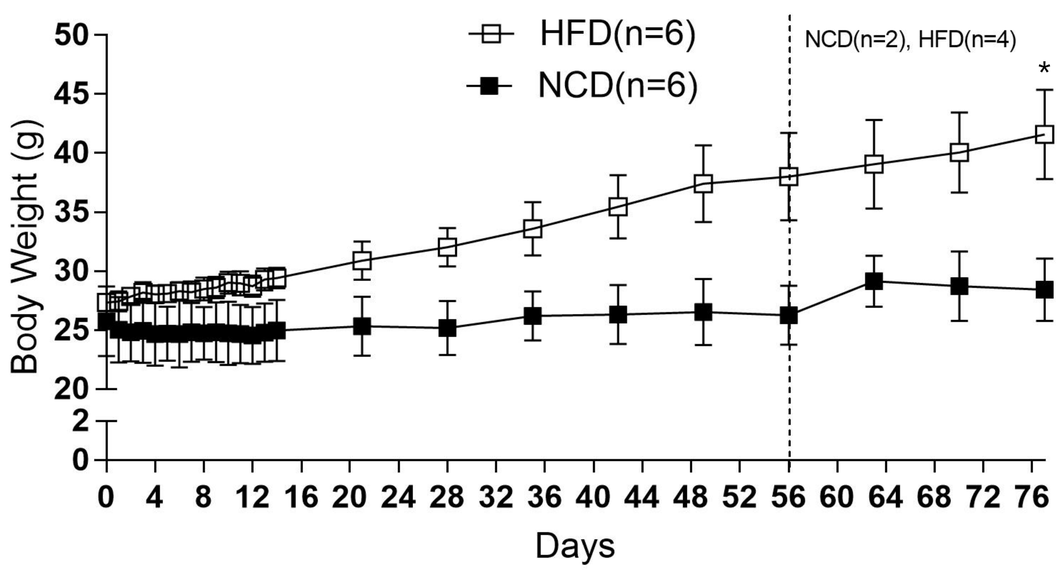
INTRODUCTION

The primary model for inducing cardiac dysfunction in mice requires surgical transverse aortic constriction (TAC). However, this method of inducing cardiac dysfunction is limited to a narrow model of cardiac dysfunction, one that does not consider common co-morbidities of heart failure, including obesity and type 2 diabetes. Current studies using mouse models show that metabolic syndrome is linked to heart failure with preserved ejection fraction (HFpEF), while others indicate that high fat diet alone in a mouse model can induce diastolic dysfunction. Alternatively, other studies indicate that diabetes and adipose dysfunction do not induce hypertension in a rat model. Therefore, developing a mouse model to explore the connection between metabolic and cardiac dysfunction is critical to exploring potential overlapping pathways that are contributing to this co-morbidity. Similarly, developing a model that induces a more clinically relevant metabolic and cardiac pathology could help develop novel integrative therapies that address both diseases. In this study, we hypothesize that high fat diet alone can induce both metabolic and cardiac dysfunction. Ultimately, findings from this preliminary study will be important for ongoing research into developing a mouse model with cardiac and metabolic dysfunction, and exploration of their overlapping pathways.

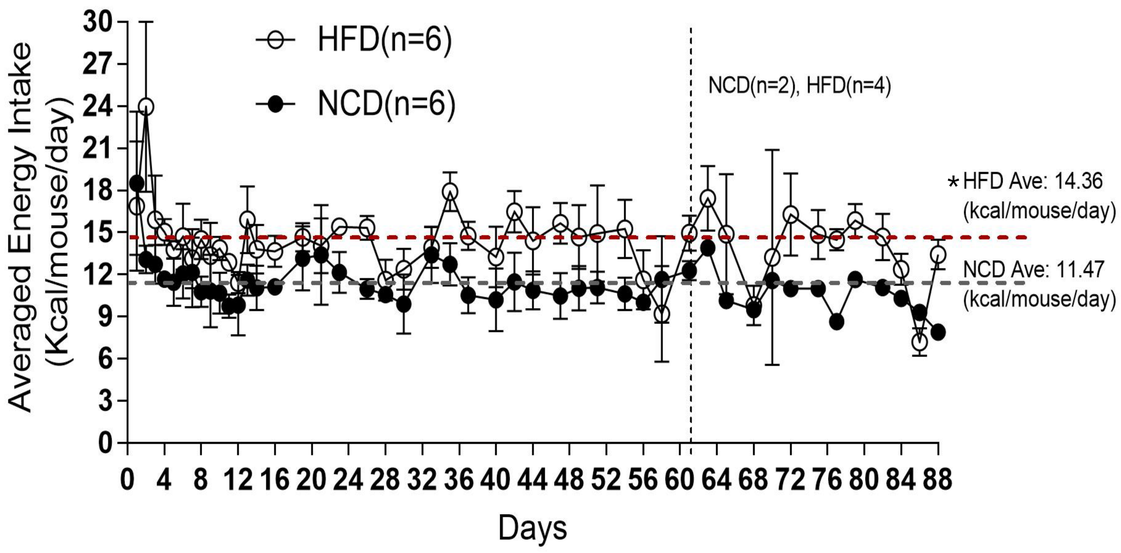
RESULTS

Figure 1. Body Weight and Energy Consumption

A. Body Weight *P<0.05



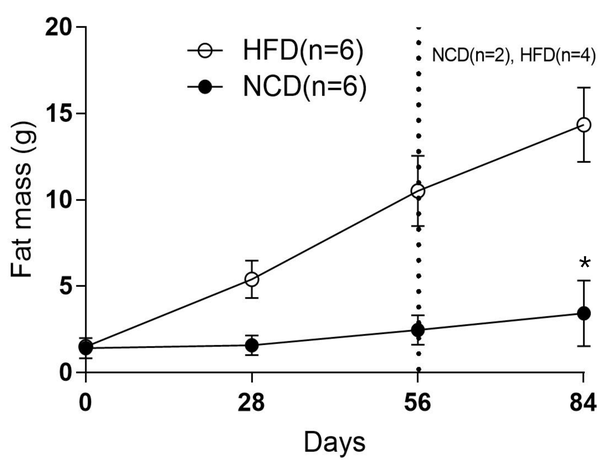
B. Energy Consumption *P<0.05,



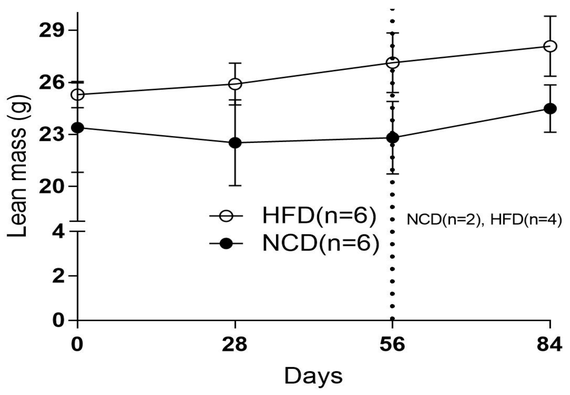
1A. Body weight was measured at the same time each day. Body weight increased significantly more in the HFD group compared to the NCD group (p=0.013). 1B. Daily food intake measurements were used to calculate energy consumption. As expected energy consumption was consistently higher in the HFD group (p=0.0001). Data is presented as mean±SEM. Data was analyzed using a T-test.

Figure 2. Echo MRI Body Composition

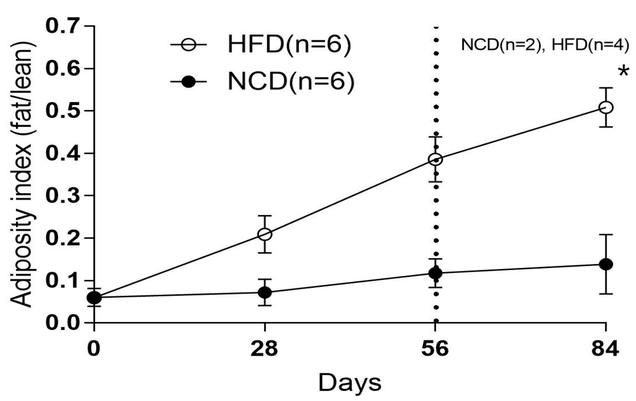
A. Fat Mass % *P<0.05



B. Lean Mass % P=ns

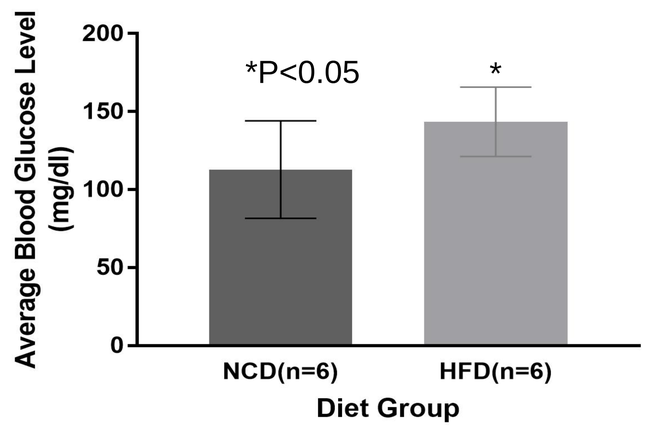


C. Adiposity Index *P<0.05



All body composition data was collected using EchoMRI. 2A. HFD mice had increased body fat mass percentage (p=0.0038) 2B. HFD and NCD mice had no statistically significant differences in lean mass percentage (p=0.317). 2C. HFD mice had a significant increase in adiposity index. (p=0.0013). Data is presented as mean±SEM. Data was analyzed using a T-test.

Figure 3. Fasting Glucose Levels



3. Glucose levels at 8 week were measured after 14hours of overnight fasting. Fasting glucose levels were significantly higher in mice fed HFD (p=0.032). Data is presented as mean±SEM. Data was analyzed using a T-test.

CONCLUSIONS

In summary, the preliminary data collected in this study supports our hypothesis that high fat diet alone induces metabolic dysfunction in mice. Mice in the HFD group had significantly higher body weight and body fat composition. Moreover, mice in the HFD group showed signs of metabolic dysfunction, specifically higher fasting blood glucose levels compared to NCD mice. The future direction of this project is to consider a group of free fatty acid receptor 4 (Ffar4) knockout mice. Since Ffar4 is expressed in both cardiac myocytes and adipose tissue evaluating the role of this receptor in metabolic and cardiac dysfunction would present greater insight into the underlying mechanisms of their co-morbidity. Moreover, since our lab found that Ffar4 is required for the cardio protective effects of omega-3-polyunsaturated fatty acids (ω3-PUFAs) in the heart, additional investigation will consider potential metabolic and cardio protective effects of mice fed supplemental ω3-PUFA diet. Ultimately, if Ffar4 is required for the cardio protective effects of ω3-PUFAs in the heart as well as in adipose tissue, exploring the link between cardiac and adipose function may provide important evidence regarding the underlying mechanisms of Ffar4 mediated ω3-PUFA signalling, and offer novel treatments for heart failure and its associated comorbidities, diabetes and obesity.

ACKNOWLEDGEMENTS

The authors would like to thank Pilar Ariza Guzman, DVM, Manager of Physiology Core Labs in the Department of Integrative Biology and Physiology for EchoMRI measurements.